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Bloodstream infections: Epidemiology, risk factors, and resistance profiles in a university hospital: A five-year cross-sectional analysis

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Abstract

Aim: Bloodstream infections present a significant healthcare challenge, causing substantial morbidity and mortality despite advancements in antimicrobial therapy. This study, conducted at the Infectious Diseases and Clinical Microbiology Clinic at Ondokuz Mayıs University (OMU), aimed to evaluate epidemiological characteristics, risk factors, infectious agents, and resistance profiles in hospitalized patients with bloodstream infections.

Material and Methods: This cross-sectional prospective analysis encompassed adult patients admitted to OMU between 2015 and 2019. Data included susceptibility tests, infection focus, treatments, and patient survival. Patients were categorized as having bacteremia or sepsis. Blood culture samples were collected with strict sterile procedures.

Results: Of the 100 patients, 47 had community-acquired infections, and 53 had nosocomial infections. The most common community-acquired focus was the urinary system (42.6%), and the most common nosocomial focus was intravenous catheters (43.4%). Escherichia coli (E. coli) was the most common causative microorganism, with 23% prevalence. Extended-spectrum beta-lactamase (ESBL) was detected in E. coli (34.7%) and multi-drug resistance in 47.8%. Klebsiella spp. exhibited ESBL (61.5%), multi-drug resistance (38.4%), carbapenem resistance (23%), and other resistances. Staphylococcus aureus had 28.5% methicillin resistance.

Discussion: This study offers vital insights into bloodstream infections, revealing their prevalence, causes, and resistance patterns. The challenge of drug-resistant organisms, especially ESBL and carbapenem-resistant bacteria, emphasizes the need for tailored treatment strategies and collaborative efforts. The increasing prevalence of MRSA and VRE underscores the importance of prudent antibiotic use and rigorous infection control. In conclusion, this study calls for a collective approach to address evolving risks in bloodstream infections, improving patient outcomes and public health.

Keywords

Bloodstream Infections, Community Acquired Infections, Nosocomial Infections, Antibiotic Resistance

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Introduction

Bloodstream infections, despite aggressive broad-spectrum antimicrobial therapies and supportive care, remain a formidable challenge, contributing significantly to morbidity and mortality rates[1]. According to the Centers for Disease Control and Prevention (CDC), rising rates of antibiotic resistance add a layer of complexity to the management of these life-threatening infections (Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/). It has therefore become more important to rigorously study the infectious agents that cause these conditions and to develop stronger measures for accurate diagnosis and effective treatment.

While the spectrum of pathogens causing bloodstream infections may fluctuate over time, bacteria continue to dominate as the primary culprits [2,3]. The stealthy presence of viruses often eludes diagnosis, further complicating the scenario [4]. Gram-negative bacteria typically take center stage, but the surge in gram-positive bacterial infections, driven by the increasing prevalence of interventional procedures, warrants close attention [5]. Additionally, the past decade has witnessed a notable upsurge in bloodstream infections caused by fungal agents, underscoring a shifting landscape [6]. Furthermore, it is crucial to recognize that the identities of isolated infectious agents and their susceptibility profiles exhibit considerable variation, contingent upon the demographic attributes of patients and the specific treatment regimens employed [7]. As a result, maintaining a watchful eye on these infections is of utmost importance, as it paves the way for the implementation of tailored empirical treatments aligned with the unique profiles of individual patients [8].

This study, conducted at the Infectious Diseases and Clinical Microbiology Clinic at the Ondokuz Mayıs University, sets out with a clear aim: to comprehensively assess the epidemiological characteristics, risk factors, infectious agents, and their resistance profiles in patients hospitalized with bloodstream infections. The overarching objective is to furnish a comprehensive understanding of these infections, offering insights into their prevalence, etiology, and the pressing matter of resistance. The findings from this research promise to significantly inform and enhance medical practices in this vital field of healthcare.

Material and Methods

This study presents the results of research conducted within the framework of the thesis titled 'Causative Agents and Resistance Issues in Community-Acquired and Nosocomial Sepsis.

Study Design: This cross-sectional prospective analysis encompassed adult patients (age > 18 years) admitted to Ondokuz Mayıs University's Infectious Diseases and Clinical Microbiology service between 2015 and 2019. The study group included 100 patients, comprising 45 males and 55 females from diverse age groups. Patients were included based on the presence of causative microbial growth in their blood cultures.

Data Recording: Susceptibility tests were conducted on the causative microorganisms isolated from blood cultures, and the infection focus was documented. Coagulase-negative staphylococci that grew only once were not considered causative unless subsequent growth was consistent with clinical condition and similar sensitivity. For catheter-related infections, microorganisms exhibiting the same causative agent and sensitivity were regarded as significant if they concurrently grew in blood culture. Detailed records of antibiotic and supportive treatments, as well as patient survival status, were maintained. Day 0 was defined as the day when microorganisms were detected or growth signals observed, followed by comprehensive systemic evaluations.

Classification: Patients with microbial growth in blood cultures were classified as having bacteremia, while those with bacteremia and a SIRS score of 2 or higher were categorized as sepsis cases. Septic shock was defined for sepsis patients exhibiting hypotension requiring vasopressors to maintain a mean arterial pressure of ≥65 mmHg and serum lactate levels exceeding 2 mmol/L (18 mg/dl).

Blood Culture Collection: Blood culture samples were obtained by drawing blood from at least two distinct veins, with a 20-minute interval between samples, prior to initiating antibiotic therapy to prevent treatment delay. A rigorous cleansing process with 70% alcohol and 10% povidone iodine was performed at the puncture site before blood sample collection. A minimum of 10 ml of blood was collected. To maintain sterility, the rubber stopper of the blood culture bottle was disinfected with alcohol after removing the plastic cap, placed into the blood culture bottle, and wiped with alcohol once more.

Microbiological Analysis: Blood culture bottle growth was monitored using the automated BD BACTEC™ system (Becton Dickinson, Sparks, MD, USA). Bacterial identification was conducted with the VITEK®MS system (bioMérieux, France), and antibiotic susceptibility tests were carried out with the VITEK®2COMPACT device (bioMérieux, France). Extended-spectrum beta-lactamase (ESBL) identification was confirmed via double-disc synergy testing, following EUCAST standards for antibiotic susceptibility tests and ESBL enzyme identification.

Data Analysis

Statistical Analysis: Statistical analyses were performed using IBM SPSS 22 software. Sociodemographic characteristics of the patients were subjected to frequency analysis. Independent two-sample t-tests were used for normally distributed and binary variables, while non-normally distributed binary variables were analyzed with the Mann-Whitney U test. The Friedman test was applied for non-normally distributed dependent groups with more than two repetitions. Qualitative variable relationships were assessed using the Pearson Chi-Square test. All statistical tests were conducted at a 95% confidence level.

Ethical Approval

This study was approved by the Ethics Committee of Ondokuz Mayıs University, Faculty of Medicine (Date:14.05.2015 , No: OMÜ KAEK 2015/230).

Results

Out of 100 patients, 45% of patients were females (n=45), and 55% were males (n=55), with an average age of 62.93 ± 15.84 years. Among them, 47% (n=47) presented with community-acquired infections, while 53% (n=53) had nosocomial infections. The mean age for patients with community-acquired infections was 62.19 ± 17.62 years, and for those with nosocomial infections, it was 63.58 ± 14.22 years. There was no statistically

significant age difference between these two groups (p=0.663). When examining the comorbidities of the patients, it was found that in the community-acquired infections group, 12 patients (25.5%) had diabetes mellitus (DM), whereas in the nosocomial infections group, 16 patients (30.2%) had DM. There was no statistically significant difference in terms of DM between the groups (p>0.05). However, in terms of chronic kidney disease (CKD), 7 patients (14.9%) in the community-acquired infections group had CKD, while 22 patients (41.5%) in the nosocomial infections group had CKD. A statistically significant difference was observed in CKD between the two groups (p=0.007). There were no statistically significant differences between the groups regarding other comorbidities, including chronic liver disease (CLD), congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), immunosuppressive therapy (IS therapy), and hypertension (HTN) (p>0.05).

In our study, we investigated the spectrum of causative microorganisms in bloodstream infections, focusing on their differentiation between nosocomial and community-acquired cases among 100 patients. Notably, Escherichia coli emerged as the predominant pathogen, responsible for 23% of all cases. However, the distribution of causative microorganisms revealed striking disparities between nosocomial and community-acquired infections. Within nosocomial infections (53% of the cases), Escherichia coli remained a significant contributor, causing 13.2% of these cases. Staphylococcus aureus was also prevalent, responsible for 11.3% of the nosocomial infections. On the other hand, community-acquired infections saw an even higher incidence of Escherichia coli, contributing to 34% of the cases, along with 17% attributed to Staphylococcus aureus. Furthermore, skin and soft tissue infections played a substantial role in community-acquired cases, accounting for 19.1% (Table 1).

Table 1. Causative Microorganisms in Bloodstream Infections by Source

Microorganisms	Nosocomial infections n (%)	Community-acquired infections n (%)	Total n (%)
Escherichia coli	7 (13,2)	16 (34)	23 (23)
Staphylococcus aureus	6 (11,3)	8 (17)	14 (14)
Klebsiella spp.	9 (16,9)	4 (8,5)	13 (13)
Enterobacter cloacae	5 (9,4)	2 (4,2)	7 (7)
Staphylococcus epidermidis	4 (7,5)	2 (4,2)	6 (6)
Proteus mirabilis	2 (3,7)	3 (6,4)	5 (5)
Enterococcus spp.	4 (7,5)	1 (2,1)	5 (5)
Pseudomonas aeroginosa	4 (7,5)	1 (2,1)	5 (5)
Streptococcus pneumonia	2 (3,7)	2 (4,2)	4 (4)
Acinetobacter spp.	3 (5,6)	1 (2,1)	4 (4)
Staphylococcus sciuri	1 (1,8)	0 (0)	1 (1)
Streptococcus viridans	0 (0)	1 (2,1)	1 (1)
Sthenotrophomonas maltophilia	1 (1,8)	0 (0)	1 (1)
Providencia rettgeri	1 (1,8)	0 (0)	1 (1)
Listeria monocytogenes	0 (0)	1 (2,1)	1 (1)
Corynebacterium striatum	0 (0)	1 (2,1)	1 (1)
Citrobacter freundii	1 (1,8)	0 (0)	1 (1)
Morganella morganii	0 (0)	1 (2,1)	1 (1)
Salmonella spp.	0 (0)	1 (2,1)	1 (1)
Streptococcus agalactia	0 (0)	1 (2,1)	1 (1)
Serratia marcescens	1 (1,8)	0 (0)	1 (1)
Achromobacter xylosoxidans	1 (1,8)	0 (0)	1 (1)
Candida albicans	1 (1,8)	0 (0)	1 (1)
Criptococcus neoformans	0 (0)	1 (2,1)	1 (1)
Total	53 (53)	47 (47)	100

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Table 2. Distribution of patients according to the focus of infection.

Source of Infection	Community-acquired infections n (%)	Nosocomial infections n (%)	Total n (%)
Urinary system	20 (42.6)	14 (26.4)	34 (34)
Intravenous Catheter	1 (2.1)	23 (43.4)	24 (24)
Skin-Soft tissue	9 (19.1)	6 (11.3)	15 (15)
Lung	3 (6.4)	3 (5.7)	6 (6)
Central nervous system	4 (8.5)	1 (1.9)	5 (5)
Other	4 (8.5)	4 (7.5)	8 (8)
Isolated Bacteremia	6 (12.8)	2 (3.8)	8 (8)
Total	47 (47)	53 (53)	100 (100)

Table 3. Microorganism Resistance Profiles in Bloodstream Infections

Microorganisms	Resistance profiles	n	%
Esherichia coli	ESBL (+)	8	34,7
	ESBL (-)	15	65,3
	MDR (+)	11	47,8
	MDR (-)	12	52,2
	Carbapenem resistance (+)	0	0
	XDR (+)	0	0
	XDR (-)	23	100
	PDR (+)	0	0
	PDR (-)	23	100
Klebsiella spp.	ESBL (+)	8	61,5
	ESBL (-)	5	38,5
	MDR (+)	5	38,4
	MDR (-)	8	61,6
	Carbapenem resistance (+)	3	23,1
	XDR(+)	1	7,6
	XDR (-)	12	92,4
	PDR(+)	1	7,6
	PDR(-)	12	92,4
Acinetobacter spp.	MDR (+)	1	25
	MDR (-)	3	75
	Carbapenem resistance (+)	3	75
	XDR(+)	0	0
	XDR (-)	4	100
	PDR(+)	1	25
	PDR(-)	3	75
Nosocomial infections	ESBL (+)	13	50
	ESBL (-)	13	50
Community based infections	ESBL (+)	8	33,3
	ESBL (-)	16	66,7
Carbapenem resistance (+)	Klebsiella spp.	7	46,7
	Acinetobacter spp.	6	40
	Providencia rettgeri	2	13,3

ESBL:Extended spectrum betalactamases; MDR:Multi drug resistance, PDR:Pan drug resistance; XDR:Extreme drug resistance

As depicted in Table 2, among patients with community-acquired infections, the most common primary sources of infection were the urinary tract (42.6%, n=20) and skin and soft tissue (19.1%, n=9). Conversely, for patients with nosocomial infections, intravenous catheters (43.4%, n=23) and urinary tract (26.4%, n=14) stood out as the predominant sources of infection.

In our comprehensive analysis of bloodstream infections, we observed distinctive resistance patterns among Escherichia coli, Klebsiella spp., and Acinetobacter spp., categorized by nosocomial and community-based infections. Among Escherichia coli cases, 34.7% (n=8) were ESBL-positive, while 65.3% (n=15) were ESBL-negative. Additionally, 47.8% (n=11) exhibited multi-drug resistance (MDR), and the remaining 52.2% (n=12) were MDR-negative, notably showing no carbapenem resistance. Klebsiella spp. presented a higher prevalence of ESBL-positive cases, with 61.5% (n=8), and 38.5% (n=5) were ESBL-negative. Among them, 38.4% (n=5) showed MDR, while 61.6% (n=8) were MDR-negative. Notably, 23.1% (n=3) displayed carbapenem resistance, and 7.6% (n=1) exhibited extreme drug resistance (XDR) and pan drug resistance (PDR). In the case of Acinetobacter spp., 25% (n=1) showed MDR, while the remaining 75% (n=3) were MDR-negative, and all cases displayed carbapenem resistance. Furthermore, when considering nosocomial and community-based infections, ESBL-positive cases were equally distributed, with 50% (n=13) in each group. Carbapenem resistance was observed in 46.7% (n=7) of community-based Klebsiella spp. infections, 40% (n=6) in Acinetobacter spp., and 13.3% (n=2) in Providencia rettgeri (Table 3).

Discussion

Bloodstream infections, affecting over 30 million people worldwide, remain a significant global health challenge, causing substantial morbidity and mortality despite ongoing medical advancements [9]. With increasing life expectancy, individuals are increasingly exposed to the risk of infection. Westphal et al.'s study, akin to ours, found that both community-acquired and nosocomial infections predominantly affect individuals aged 60 or older. This higher average age can be attributed to the greater prevalence of chronic diseases and age-related weakening of the immune system, which elevates the susceptibility to infections. Furthermore, advanced age often necessitates more invasive medical interventions, which, in turn, heightens the risk of infection [10].

In another retrospective study by Rhee et al., intra-abdominal infections were identified as the most common source (20.6%) of nosocomial infections, followed by pneumonia, urinary tract infections, and less common soft tissue infections [11]. Similarly, a retrospective analysis of community-acquired bloodstream infections in our country revealed urinary tract infections (45%), pneumonia (18%), intra-abdominal infections (9.6%), and skin and soft tissue infections (5%) as the primary sources [12]. It is noteworthy that our study pinpointed urinary tract infections and skin and soft tissue infections as predominant sources in community-acquired cases. The differences in infection source rankings can be attributed to our comprehensive approach, which involved managing patients admitted to the infectious diseases service, as opposed to cases managed by different clinics and consultation services for lung and abdominal infections. This highlights the critical need for tailored treatment strategies and interdisciplinary collaboration to address these infections.

The Extended Prevalence of Infection in Intensive Care (EPIC) study, utilizing the point prevalence method, reported lung infections accounting for 64% of cases in intensive care units, followed by abdominal infections (20%), vascular catheter-related infections (15%), and genitourinary system infections (14%) [13]. Pneumonia was the most frequent infection, followed by vascular catheter-related and urinary system infections. Conversely, our study, focusing on patients admitted to the infectious diseases service, highlighted the predominance of vascular catheter-related infections since patients diagnosed with pneumonia were typically managed by pulmonary diseases clinics or anesthesia/internal medicine intensive care units. The growing number of dialysis patients, requiring vascular catheters, emphasized the prominence of vascular catheter-related infections in our study, ultimately making them the leading cause of hospital-acquired infections.

Bacterial infection rates in these patients were found to be 30-66.4%. In a study conducted in our country, culture growth was found in 46.5% of the total patients, 45.5% of the patients hospitalized in the chest diseases service with chronic obstructive pulmonary disease (COPD) attack and 52.5% of the patients hospitalized in the intensive care unit [14]. Similarly, our study significantly increases the risk of COPD, especially community-acquired infections.

When analyzing the microbial agents responsible for bloodstream infections, a study conducted in our country reported Klebsiella pneumoniae and Escherichia coli as the most common gram-negative pathogens in blood cultures [15]. Meanwhile, Staphylococcus aureus was the predominant gram-positive pathogen. In our study, Escherichia coli was the most common gram-negative agent, but when distinguishing between community-acquired and nosocomial infections, Klebsiella spp. became the primary pathogen in nosocomial cases. A similar study focusing on community-acquired infections in the elderly also identified Escherichia coli as the most common pathogen, aligning with our findings [16]. The similarities in results are likely due to the majority of patients in our study being managed in the intensive care unit.

The emergence of Extended-Spectrum Beta-Lactamases (ESBL) in E. coli and Klebsiella species, attributed to their ability to spread among strains, is a notable concern. ESBL rates can vary between outpatients and inpatients, the types of samples from which strains are isolated, whether the agent is nosocomial, and over the years [17]. Although our study didn't show a statistically significant difference, the rate of ESBL in community-acquired infections was 33%, while it nearly doubled in hospital-acquired infections, potentially indicating a more resistant profile in the latter.

Carbapenem resistance was not detected in E. coli strains from two separate studies involving urinary tract infections in our country, aligning with our findings [18]. This may be due to the limited use of carbapenems, especially in outpatients, due to their parenteral administration

In ESBL-positive K. pneumoniae and K. oxytoca strains,

carbapenems are highly effective, particularly after amikacin. However, the overuse of carbapenems without adhering to rational antibiotic use policies can lead to resistance development. Studies conducted in our country by Görgec et al. and Copur et al. found that ESBL-positive K. pneumoniae isolates exhibited resistance rates of approximately 5% for imipenem and meropenem [19,20]. In our study, we also detected carbapenem resistance, with a rate of 7%, which aligns with previous research. While carbapenem resistance remains lower than ESBL resistance, it's noteworthy that it has increased compared to the past. This emphasizes the importance of considering this trend, especially when making empirical treatment choices [21]. Both studies identified a history of hospitalization as a risk factor for carbapenem resistance in Acinetobacter spp. strains. In our study, Acinetobacter spp. was one of the two carbapenem-resistant agents. This highlights the significance of rational antibiotic use, as carbapenem-resistant Acinetobacter spp. strains are increasingly observed in ward patients, extending beyond the confines of intensive care units.

The rate of antibiotic use is increasing, and this increase brings along drug resistance. Therefore, antibiotic treatment strategies need to be reconsidered. In our study, it was determined that a history of antibiotic use was a risk factor for the development of infection with both ESBL-positive and other multi-drug resistant agents. The history of hospitalization, which is frequently mentioned in the literature, was also examined by us, but although ESBL is more common in patients with a history of hospitalization, no statistically significant difference was found in terms of resistance development.

It draws attention with different studies that resistance to methicillin in staphylococci has increased over the years: In different studies, MRSA rates were found to be 31.7% in 1988, 35.3% in 1992, 31.6% in 1994, 36.1% in 1998, 60.2% in 2000, and 64% in 2001. Grundmann et al.[22] On the other hand, in the study they conducted between 1999 and 2002, they found the rate of MRSA to be 5-20% [23]. The low is quite remarkable. In our study, this rate was determined as 28.5%, and although it seems to be an average value according to sample studies, it is quite remarkable that this rate was much lower in the past years.

In a study conducted in our country for Enterococcus strains, penicillin resistance was found to be 48%, ampicillin resistance was 43% in samples taken from outpatients, and vancomycin and teicoplanin resistance were not detected. Penicillin resistance was found to be 84%, ampicillin resistance to 70%, and vancomycin and teicoplanin resistance to 5% in the samples sent from hospitalized patients [24]. Although we had lower ampicillin resistance compared to the sample study, vancomycin resistance was much higher with 20%. Today, patients are colonized and infected with vancomycin-resistant enterococci in many countries. These infections are increasing due to non-compliance with rational antibiotic use policies. Therefore, it is important to detect resistant strains and to know their resistance rates.

Conclusion:

In summary, this study underscores the growing challenge of bloodstream infections, especially those caused by drug-resistant organisms. To combat this threat, we must prioritize rational antibiotic use, enhance infection control measures, and foster interdisciplinary collaboration. Addressing these issues collectively is essential for improving patient outcomes and safeguarding public health.

Limitations

This study has some limitations. Firstly, the fact that the research was conducted at a single medical center and had a limited sample size may limit the generalizability of the results. Additionally, epidemiological changes during the data collection period or changes in hospital practices could impact the findings. The retrospective nature of the data used in the study may increase the possibility of data gaps or inaccuracies. Finally, relying on data from only one medical center may lead to different results in different geographical regions or healthcare systems. Therefore, conducting similar studies in different centers with larger sample groups is crucial for obtaining more reliable results.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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